benzene, yellow needles (from C_2H_5OH–$CHCl_3$); mp 258–262 °C: IR 1650 (amide CO), 760 cm^{-1}; Bruker NMR ($CDCl_3$ + TFA to clear) δ 2.78 (s, 3 H, $ArCH_3$), 4.15 (s, 3 H, NCH_3), 4.96 (s, 2 H, $ArCH_2Cl$), 7.3–7.7 (m, 2 H, ArH), 7.8–8.0 (m, 1 H, 7-H), 8.25–8.4 (m, 1 H, 10-H); MS, *m/e* 363 (3Cl, M^+), 328 (2Cl, M – 35).

1,6-Dichloro-3,4,5-trimethylindeno[1,2,3-*de*]quinolin-2-(3*H*)-one (7b). Dihydroquinolinone **2e** (80 mg) was covered with concentrated H_2SO_4 (0.5 mL) and the permanganate-colored mixture was stirred and heated at 80–85 °C for 5 min; the reaction mass turned orange and liberated HCl. After having been cooled somewhat, water was added and the canary-yellow solid was collected by filtration, washed with water, and dried at 50 °C (60 mg; TLC [benzene–C_2H_5OH (100:1) or $CHCl_3$] showed virtually only **7b**), yellow crystals (from $CHCl_3$–C_2H_5OH), mp 291–293 °C: IR 1635 (amide CO) cm^{-1}; Bruker NMR δ 2.47 (s, 3 H, $ArCH_3$), 2.59 (s, 3 H, $ArCH_3$), 3.86 (s, 3 H, NCH_3), 7.4–7.5 (m, 2 H, ArH), 8.2–8.3 (m, 2 H, ArH); MS, *m/e* 329 (2Cl, M^+), 314 (2Cl, M – 15), 294 (1Cl, M – 35).

Action of H_2SO_4 on 5. 4-Hydroxydihydroquinolinone **5** (100 mg) was reacted (for 2 min, no Ag_2SO_4) with concentrated H_2SO_4 (0.3 mL) as described for **2b**; a parallel and control run was conducted with **2b** 100 mg). The washed and dried ($MgSO_4$) $CHCl_3$ extract (15 mL) from **5** was examined by TLC [benzene–acetone (10:1) and $CHCl_3$] which revealed a product mixture (of **6** and **7**) virtually identical in composition with that derived from **2b**.

Registry No. **1b** (noncoordinate entry), 98539-86-7; **1b** (coordinate entry), 98526-28-4; **1b** (R = H) (noncoordinate entry), 98526-11-5; **1b** (R = H) (coordinate entry), 68682-89-3; **1c** (noncoordinate entry), 98526-08-0; **1c** (coordinate entry), 98526-29-5; **1c** (R = H) (noncoordinate entry), 98526-12-6; **1c** (R = H) (coordinate entry), 98526-31-9; **1d** (noncoordinate entry), 98526-09-1; **1d** (coordinate entry), 68682-93-9; **1d** (R = H) (noncoordinate entry), 98526-13-7; **1d** (R = H) (coordinate entry), 98539-87-8; **1e** (noncoordinate entry), 98526-10-4; **1e** (coordinate entry), 98526-30-8; **1e** (R = H) (noncoordinate entry), 98526-14-8; **1e** (R = H) (coordinate entry), 98526-32-0; **2b**, 98526-17-1; **2c**, 98526-21-7; **2d**, 98526-24-0; **2e**, 98526-20-6; **3** (R = Me, R^1 = *p*-$NO_2C_6H_4$, R^2 = H), 98526-22-8; **3** (R = Me, R^1 = *p*-$NO_2C_6H_4$, R^2 = Cl), 98526-23-9; **3a**, 98526-15-9; **3b**, 98526-16-0; **4**, 98526-18-2; **5**, 98526-19-3; **6**, 98526-25-1; **7a**, 98526-26-2; **7b**, 98526-27-3.

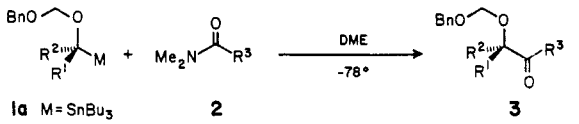
Communications

A Trialkylstannane-Mediated Approach to Acyloin Products

Summary: α-Alkoxy organolithium compounds, generated through the treatment of the corresponding tri-*n*-butylstannane with *n*-BuLi, smoothly condense with *N,N*-dimethylamides to afford α-alkoxy carbonyl products. This condensation is functionally equivalent to a regiocontrolled acyloin condensation.

Sir: Contemporary targets of total synthesis have stimulated intense interest in the development of carbon–carbon bond-forming processes that generate carbon skeletons bearing a variety of oxygenation patterns. Impressive advances have been recorded for the assembly of substrates bearing 1,3-oxygen relationships through the aldol condensation[1] and related methodologies.[2] In contrast, relatively less study has been devoted toward the realization of general methods of forming carbon–carbon bonds resulting in vicinal oxygenation.[3,4] Given the synthetic versatility of α-alkoxy carbonyl compounds,[5] the bond-forming strategy embodied in the acyloin condensation[6] offers an attractive approach to compounds bearing contiguous oxygen substitution. With this in mind, we wish to report on a trialkylstannane-mediated condensation that efficiently affords protected α-alkoxy carbonyl products in a manner formally equivalent to an acyloin condensation.

Table I. Intermolecular Acylation of α-Alkoxy Organolithium Species 1b[a]



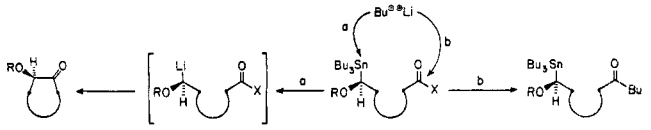
1a M = $SnBu_3$ 2 3

1b M = Li

entry	R^1	R^2	R^3	yield,[b] %
1	C_2H_5	H	H	67
2	Me_2CH	H	H	78
3	Me_2CH	H	Ph	74
4	Me_2CH	H	C_2H_5	67
5[c,d]	Ph	Me	C_2H_5	63
6	$CH_2(CH_2)_3CH_2$		C_2H_5	68
7	Me_2CH	H		80[e]

[a] 1a (M = $SnBu_3$) → 1b (M = Li) via 1 equiv of *n*-BuLi, DME, −78 °C. [b] After column chromatography. [c] Using the methoxymethyl protecting group. [d] M = $SnMe_3$ in 1a. [e] Isolated as a mixture of diastereomers.

Scheme I



(1) For recent reviews, see: (a) Heathcock, C. H. In "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 2, Chapter 2. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (c) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203.

(2) For recent examples, see: (a) Hoffman, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (c) Meyers, A. I.; Yamamoto, Y. *Tetrahedron* **1984**, *40*, 2309.

(3) (a) Abdel-Magid, A.; Lantos, I.; Pridgen, L. N. *Tetrahedron Lett.* **1984**, 3273. (b) Seebach, D.; Naef, R.; Calderari, G. *Tetrahedron* **1984**, *40*, 1313. (c) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988. (d) Stevens, R. W.; Mukaiyama, T. *Chem. Lett.* **1983**, 595. Other examples may be found in ref 1 and 2.

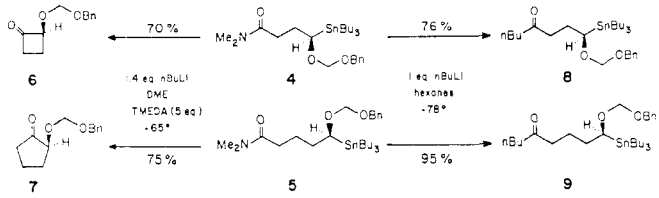
(4) (a) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1982**, *47*, 5420. (b) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

(5) For use as asymmetric electrophiles, see: (a) Eliel, E. L. In "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 2, Chapter 5. (b) Fujita, M.; Hiyama, T. *J. Am. Chem. Soc.* **1984**, *106*, 4629. (c) Oishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 338. For use as asymmetric nucleophiles, see ref 1.

(6) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React. (N.Y.)* **1976**, *23*, 259.

0022-3263/85/1950-4655$01.50/0

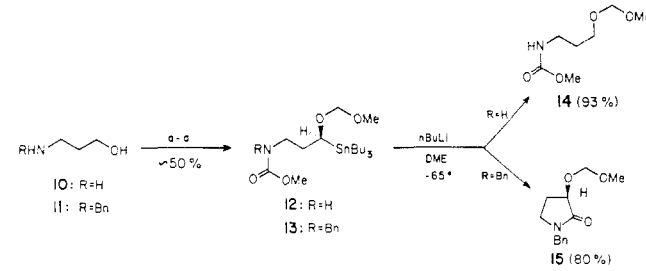
Scheme II



We envisioned a direct synthesis[7] of these compounds through acylation of stereodefined α-alkoxy organolithium species which, in turn, are efficiently prepared through stereospecific tin–lithium exchange of readily accessible α-alkoxy organostannane precursors (e.g., **1a** → **1b**).[4,8] A survey of potential acylating reagents revealed that simple *N,N*-dimethylamides smoothly condensed with these carbanions in the desired manner without complication by products resulting from overaddition. As the results in Table I indicate, this approach allows the convergent preparation of protected acyloin products **3** with unambiguous placement of functionality and promising generality. The successful acylations with highly substituted carbanions are notable (entries 5 and 6) and indicative of the relatively high nucleophilic character of these α-alkoxy carbanions in comparison with unfunctionalized organolithium species.[9]

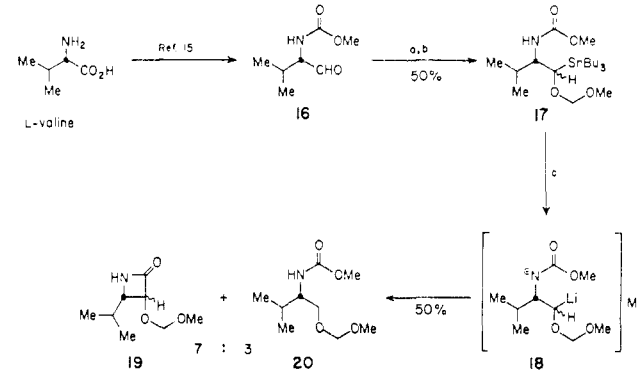
Of particular interest to us was the extension of this methodology to the preparation of cyclic products through an intramolecular acylation of these α-alkoxy carbanions. This proposal requires that *n*-BuLi show a kinetic preference for tin–lithium exchange (path a) over addition to the electrophilic acyl function (path b, Scheme I).[11] To pose this question, homologous substrates **4** and **5** were prepared from γ-butyrolactone and δ-valerolactone, respectively (Scheme II).[12] Initial attempts to effect cyclization of these stannyl amides with *n*-BuLi in THF resulted in competitive reaction at both electrophilic sites (paths a and b). Further experimentation revealed, however, that clean formation of cyclic ketones **6** and **7** could be realized through treatment with a modest excess of *n*-BuLi in DME/TMEDA.[13] This reaction pathway could be completely suppressed in favor of intermolecular acylation products **8** and **9** by simply running the reaction in hexanes. The complete control over the site of butyl anion attack is probably attributable to the role of the lithium cation. In a nonpolar medium (hexanes) the amide's electrophilicity is enhanced through lithium association. Suppression of this interaction by the use of highly dissociating conditions, on the other hand, elevates the relative reactivity of the trialkylstannyl center.

Scheme III[a]



[a] (a) $ClCO_2Me$, K_2CO_3, H_2O, room temperature; (b) Me_2SO, $(COCl)_2$, Et_3N, CH_2Cl_2, room temperature; (c) $LiSnBu_3$ (2 equiv), CuBr·DMS (0.5 equiv), THF, −78 °C; (d) $MeOCH_2Cl$, *i*-Pr_2NEt, DMAP, CH_2Cl_2, room temperature.

Scheme IV[a]



[a] (a) $LiSnBu_3$ (2 equiv), THF, −78 °C; (b) $MeOCH_2Cl$, *i*-Pr_2NEt, DMAP, CH_2Cl_2, room temperature; (c) i, KH (1.8 equiv), TMEDA (4 equiv), DME, room temperature, ii, *n*-BuLi (1.9 equiv), −78 °C → room temperature.

With these results in hand, an intermolecular condensation was attempted wherein an equimolar mixture of **1a** (R^1 = Me_2CH; R^2 = H) and **2** (R^3 = C_2H_5) in DME/TMEDA was exposed to *n*-BuLi. In contrast to the intramolecular examples, 2 equiv of the alkyllithium reagent was required for complete consumption of the starting stannane **1a** which resulted in the generation of approximately equal quantities of **3** (R^1 = Me_2CH; R^2 = H; R^3 = C_2H_5) and 3-heptanone. These results indicate subtle mechanistic differences in the intramolecular and intermolecular acylation reactions that require further study for clarification.

The intramolecular acylation strategy is not reserved exclusively for the synthesis of carbocycles but also finds application to heterocycle synthesis. As an illustration, stannyl carbamates **12** and **13**, easily prepared from amino propanols **10** and **11**, respectively, were submitted to conditions of tin–lithium exchange (Scheme III). The clean formation of destannylated material **14** from the treatment of **12** with an equivalent of *n*-BuLi is indicative of a surprisingly strong kinetic preference for reaction at the tin center even in the presence of the acidic carbamate proton.[14] The desired pyrrolidone **15** is produced in high yield when proton transfer is prevented, as by benzyl substitution in **13**.

Finally, we applied this unique heterocyclic synthesis to the preparation of functionalized β-lactams. With

(7) In contrast to a multistep synthesis using acyl anion equivalents: (a) Hase, T. A.; Koskimies, J. K. *Aldrichimica Acta* **1981**, *14*, 73. (b) Hase, T. A.; Koskimies, J. K. *Aldrichimica Acta* **1982**, *15*, 35. (c) Lever, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943.

(8) For stereochemical studies, see: (a) Sawyer, J. S.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 3376. (b) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201.

(9) Successful acylations of alkyllithium compounds with dialkylamides invariably require primary organometallic reagents. An example of attempted acylation with a secondary organolithium reagent (*sec*-PrLi) with dimethylformamide reports 0% yield of the formylated product.[10] The success in the present study may be attributable to the relative stability of these anions.[8a]

(10) Evans, E. A. *J. Chem. Soc.* **1956**, 4691.

(11) For related carbocycle syntheses, see: (a) Cooke, M. P., Jr. *J. Org. Chem.* **1984**, *49*, 1144. (b) Seebach, D.; Willert, J.; Beck, A. K.; Groebel, B. T. *Helv. Chim. Acta* **1978**, *61*, 2510. (c) Boatman, R. J.; Whitlock, B. J.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 4822.

(12) Substrates **4** and **5** were prepared in excess of 65% overall yield from the corresponding lactone by the sequence: (i) Me_2NH, room temperature; (ii) Me_2SO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C; (iii) $LiSnBu_3$, THF, −78 °C; (iv) $ClCH_2OBn$, Hünig's base, DMAP, CH_2Cl_2, room temperature.

(13) All yields reported in this study are after chromatographic purification.

(14) This behavior contrasts with a recent study examining the generation of dilithio salts from β-stannyl-*N*-phenyl amides in THF/DABCO: (a) Goswami, R.; Corcoran, D. E. *J. Am. Chem. Soc.* **1983**, *105*, 7182. (b) Goswami, R.; Corcoran, D. E. *Tetrahedron Lett.* **1982**, 1463.

standard methods, L-valine was elaborated via optically pure aldehyde **16**[15] to stannyl carbamate **17** as a 1:1 mixture of diastereomers (Scheme IV).[16] Since we anticipated complications due to proton transfer and eliminative loss of the nitrogen substituent, the carbamate was deprotonated with KH prior to tin–lithium exchange.[17] The result, presumably dianion **18**, gave products **19** and **20** upon gradual warming to room temperature from which the desired β-lactam (**19**) could be isolated in yields of 30–35%. Although the mechanistic details of the conversion **17** → **19** await elucidation,[18] this preliminary example serves to illustrate a potentially useful strategy for the synthesis of optically active β-lactams from readily available α-amino acids.

The demonstration that nucleophilic α-alkoxy carbanions may be generated in the presence of mildly electrophilic acyl functionality through kinetically preferred tin–lithium exchange lays the groundwork for the design and execution of many new intramolecular processes. While the condensations in this study are functionally equivalent to the acyloin condensation, the present method is superior in its control over placement of the new carbon–carbon bond and its attendant oxygen substituents and allows the preparation of compounds that are inaccessible through acyloin methodology. Studies are under way to define the limits of functional group compatibility in intramolecular bond-forming processes and to utilize the carbon–tin bond directly in intramolecular acylations without the intermediacy of the organolithium species.

Acknowledgment is made to the National Institutes of Health for generous support of this work. We also thank J. Michael Williams for his assistance in obtaining and interpreting the NMR spectra for some of the compounds in this study.

(15) Stanfield, C. F.; Parker, J. E.; Kanellis, P. *J. Org. Chem.* **1981**, *46*, 4797.

(16) Since the main objective of this experiment was to realize cyclization of **17**, no attempt has been made to improve stereoselection in its preparation.

(17) Attempts to use excess *n*-BuLi without prior KH deprotonation under a variety of conditions failed to produce any of the desired β-lactam **19**.

(18) Perhaps bearing on this question, an intramolecular attack at a deprotonated amide carbonyl has been suggested to explain a homoenolate rearrangement.[14a]

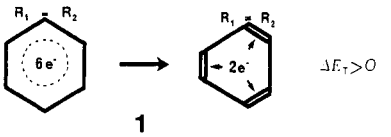
Glenn J. McGarvey,* Masayuki Kimura
Department of Chemistry
University of Virginia
Charlottesville, Virginia 22901
Received August 6, 1985

Is the Delocalized π-System of Benzene a Stable Electronic System?

Summary: Computational evidence is provided that the symmetric hexagonal structure of benzene is driven by the σ-framework alone. The π-system is found to favor a distorted and localized structure. Electronic (π) delocalization in benzene is thus forced by the σ-framework.

Sir: Why does benzene have a symmetric hexagonal geometry? According to common wisdom the tendency of the π-system to be delocalized (in "resonance") is the root cause of such a structural symmetry. This common notion has recently been questioned.[2] It was reasoned that π-delocalization cannot be the driving force for the structural features of benzene and that these features originate in the σ-framework alone, which prefers a symmetric hexagon and thereby forces the π-system to be delocalized. This communication presents computational evidence that the π-system of benzene is indeed not stable in a symmetric hexagon and that it is the σ-framework that determines the structural symmetry of benzene and forces π-delocalization.

The tendency of benzene to remain symmetric and delocalized is measured by the energy change, ΔE_T, that accompanies the localizing asymmetric distortion in **1**. It



1

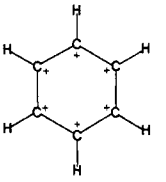
is well-known that such a distortion of benzene requires energy; i.e., $\Delta E_T > 0$ in **1**. This can be taken as evidence that the geometry and special stability of benzene are driven by the π-system that tends to cluster in a symmetric arrangement where delocalization ("resonance") of the "electronic sextet" does occur. However, while it is evident that the σ-framework, were it by itself, would favor a symmetric hexagon, there is no single proof that the π-electrons are a contributing driving force for symmetrization nor there is clear evidence that the π-system possesses an inherent tendency to be delocalized without the buttressing effect of the σ-skeleton. These tendencies must be proved or else falsified.

The total energy of benzene (at the SCF level) is expressed in eq 1. Here h_π and h_σ are the corresponding monoelectronic integrals of the π and σ MOs. The R terms

$$E_T = 2\sum_{\pi}^{occ} h_\pi + R_{\pi,\pi} + R_{\sigma,\pi} + 2\sum_{\sigma}^{occ} h_\sigma + R_{\sigma,\sigma} + V_{NN} \quad (1)$$

stand for electron–electron repulsion of a type that is specified by the subscript. The last term V_{NN} accounts for nuclear repulsion.

The first two terms in eq 1 describe the energy of the six π-electrons in the field of the bare nuclei of the C_6H_6 framework, i.e., in the field of $(C^{6+})_6(H^{1+})_6$. By adding the third term ($R_{\sigma,\pi}$) in eq 1 to the first two, the attraction of the six π-electrons to $(C^{6+})_6(H^{1+})_6$ will be partly counterbalanced by electron–electron repulsion with all the σ-type electrons (five e on each carbon and one e on each hydrogen). Therefore the first three therms in eq 1 describe the six π-electrons in the field of the σ-$(C^{1+})_6H_6$ framework which is shown in **2** and in which the charge effectively resides on the carbon atoms. Therefore the first three



2

terms of eq 1 represent the π-energy, E_π, of the six π-electrons in the field of the σ-framework which is shown in **2**. The rest of the terms in eq 1 naturally represent then

(1) Permanent address: Department of Chemistry, Ben Gurion University, Beer Sheva 84105, Israel.

(2) (a) Epiotis, N. D. *Nouv. J. Chim.* **1984**, *8*, 11. (b) Shaik, S. S.; Bar, R. *Nouv. J. Chim.* **1984**, *8*, 411. Shaik, S. S.; Hiberty, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 3089.

0022-3263/85/1950-4657$01.50/0